Synthesis of fluorinated aminosugars Positron Emission Tomography diagnostic studies

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Keywords: aminosugars, PET, diagnostic

INTRODUCTION

Aminosugars are widely spread carbohydrates in organisms, which participate in cell reorganization and signaling[1]. The involvement of these molecules in a vast variety of processes has led researches to explore their synthesis.

In this work, we developed a route to prepare fluorinated 2-acetamido-2-deoxy derivatives (Fig. 1), with potential application in ^{18}F radiolabeled sugars in cancer diagnosis and for cell mechanisms studies by Positron Emission Tomography (PET).

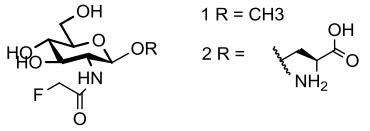
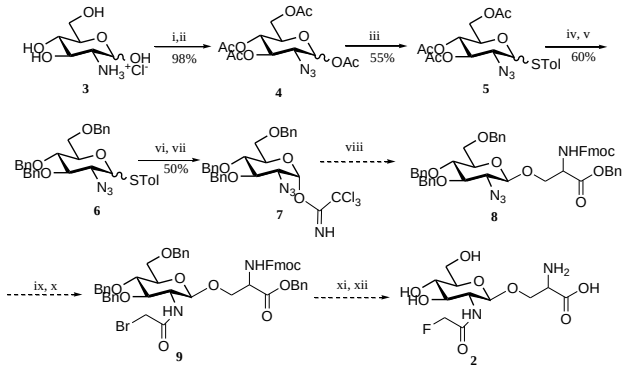


Figure 1. Fluorinated 2-acetamido-2-deoxy derivatives.

RESULTS AND DISCUSSION

In order to synthesize the fluorinated sugars having methyl or serine groups at anomeric *β*-position (as observed in the biochemical pathways) we started with the preparation the glycosyl donor **7** via a perbenzylated trichoroacetimidate (scheme 1). Thus, the commercial glucosamine hydrochloride was treating with cooper sulfate and triflic azide to give the corresponding azide, which was protected with acetyl group acetic anhydride before isolation and purification. Subsequently, the glycosylation of compound **4** with *p*-thiocresol afforded the thiosugar **5** which was treated with sodium metoxide to release the hydroxyl groups. The benzylation of the free hydroxyl groups was then performed with BnBr and NaH. Removal of the *p*-thiocresol group was achieved by *N*-iodosuccinimide and the product was functionalized in the presence of trichloroacetonitrile, DBU in DCM to give compound **7**.



Scheme 1. Reagents and conditions:i: K_2CO_3, TfN_3, ii: Ac_2O, Py, iii: p-thiocresol, $BF_3.Et_2O$, DCM, iv: NaOMe, MeOH; v: BnBr, NaH, DMF; vi: NIS, CH_3COCH_3:H_2O (9:1); vii: Cl_3CCN, DBU, DCM; viii: TMSOTf, DCM, NFmoc-Ser-OBn; ix: Ph_3P,THF, H_2O x: EDC, $BrCH_2COOH$, DMF; xi: KF, THF, xii: Pd/H_2, MeOH.

The next steps will be the glycosydic reaction to afford glicoaminoacid **8**. The azide group in position 2 of compound **8** will be reduced to amine, followed by coupling with bromoacetic acid to get **9**.Finally substitution of bromine by fluoride at the acetamide group of **9**, and OBn and Fmoc desprotection will produce the final product **2.**

CONCLUSION

The synthetic approach described in scheme 1 was very convenient to prepare the intermediate glycosyl donor **7** having O-benzyl groups. The same strategy can be pursued for derivatives of **7**, such as mannosamine and galactosamine. The final preparation of **2** via glycosylation reaction is ongoing.

ACKNOWLEDGEMENTS

Financial support from CAPES, CNPQ and FAPESP

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[1]Varki, A. et al. (Org.). 2. ed Essentials of Glycobiology. New York: Cold Spring Harbor Laboratory Press, **2009**.